AMENDMENT TO THE CLAIMS

This listing of claims will replace all prior versions of claims in the application:

Listing of Claims:

1-57 (Cancelled)

58. (Currently Amended) A product comprising a support material and a plurality of different nucleic acid molecules, wherein

the nucleic acid molecules are attached to the support material,

the nucleic acid molecules comprise a sequence which [that] is complementary to and specific for an exon or an intron of a gene and which corresponds to a region of variability due to differential splicing of said gene,

said product comprises at least two nucleic acid molecules complementary to and specific for a distinct exon or intron of the same gene,

said product allowing, when contacted with a sample containing nucleic acids under conditions [condition] allowing hybridisation to occur, the determination of the presence or absence of said exon or intron of said gene in said sample.

59. (Currently Amended) A product comprising a support material and a plurality of different nucleic acid molecules, wherein

the nucleic acid molecules are attached to the support material,

the nucleic acid molecules comprise a sequence which [that] is complementary to and specific for an exon-exon or an exon-intron junction region of a gene or RNA and which corresponds to a region of variability due to differential splicing of said gene or RNA,

said product comprises at least two nucleic acid molecules complementary to and specific for a distinct junction region of the same or a different gene or RNA,

said product allowing, when contacted with a sample containing nucleic acids under conditions allowing hybridisation to occur, the determination of the presence or absence of said junction region in said sample.

60. (Previously Presented) The product of claim 58 or 59, wherein said plurality of different nucleic acid molecules comprises cDNA molecules and is obtained by a method of identifying or cloning differentially spliced nucleic acids, said method comprising:

a) hybridizing a plurality of different RNAs derived from a first sample, wherein the composition or sequence of the RNAs is at least partially unknown, with a plurality of different cDNAs derived from a second sample, wherein the composition or sequence of the cDNAs is at least partially unknown; and

b) identifying or cloning, from the hybrids formed in a), a population of nucleic acids comprising an unpaired region, said cloned or identified nucleic acids comprising an unpaired region corresponding to portions of genes that are differentially spliced between said samples.

61. (Previously Presented) The product of claim 58, wherein said plurality of different nucleic acid molecules comprises single-stranded oligonucleotides comprising a sequence complementary to and specific for an exon or an intron of a gene, and wherein said oligonucleotides are obtained by a method comprising:

(a) identifying a splicing event characteristic of a physiopathological condition and determining the sequence of the spliced domain,

(b) synthesizing one or several single-stranded oligonucleotides complementary to and specific for said domain, and

(c) repeating steps (a) and (b) above with at least a second splicing event characteristic of said physiopathological condition.

62. (Previously Presented) The product of claim 59, wherein said plurality of different nucleic acid molecules comprises single-stranded oligonucleotides comprising a sequence complementary to and specific for junction region of a gene or RNA, and wherein said oligonucleotides are obtained by a method comprising:

(a) identifying a splicing event characteristic of a physiopathological condition and determining the sequence of the spliced domain,

(b) synthesizing one or several single-stranded oligonucleotides complementary to and specific for a junction region formed by the splicing or absence of splicing of said domain and

(c) repeating steps (a) and (b) above with at least a second splicing event characteristic of said physiopathological condition.

63. (Previously Presented) The product of claim 61 or 62, wherein the identification step (a) is based upon compilation of published sequences or sequence information from databases.

64. (Previously Presented) The product of claim 60, wherein said plurality of different nucleic acid molecules comprises an autologous nucleic acid library characteristic of alternative forms of splicings occurring between messenger and pre-messenger RNAs of a given physiological condition.

65. (Previously Presented) The product of claim 58 or 59, wherein the support material is selected from the group consisting of a filter, a membrane and a chip.

66. (Previously Presented) The product of claim 58 or 59, wherein the nucleic acid molecules comprise cDNA fragments.

67. (Previously Presented) The product of claim 58 or 59, wherein the nucleic acid molecules comprise single-stranded oligonucleotides.

68. (Previously Presented) The product of claim 67, wherein the nucleic acid molecules comprise single-stranded oligonucleotides of between 5 and 100 bases in length.

69. (Previously Presented) The product of claim 58 or 59, wherein the nucleic acid molecules are specific of alternative splicings representative of a cell or tissue in a given pathological condition.

70. (Previously Presented) The product of claim 69, wherein the nucleic acid molecules are specific of alternative splicings representative of a tumor cell or tissue.

71. (Previously Presented) The product of claim 69, wherein the nucleic acid molecules are specific of alternative splicings representative of a cell or tissue undergoing apoptosis.

72. (Currently Amended) A product for evaluating the toxicity of a compound or treatment to a cell, tissue, or organism, the product comprising a support material and a plurality of different nucleic acid molecules selected from cDNA molecules and single-stranded oligonucleotides, said nucleic acid molecules being attached to said support material, the nucleic acid molecules comprising [nucleic acid molecules containing] a sequence that is complementary to and specific for introns or exons that are retained or spliced in a cell [treated by a reference toxic compound or treatment], said product comprising at least two nucleic acid molecules complementary to and specific for a distinct exon or intron of the same gene and said product allowing, when contacted with a sample containing nucleic acids under condition allowing hybridisation to occur, the determination of the presence or absence of said exon or intron of said gene in said sample.

73. (Currently Amended) A product for evaluating the toxicity of a compound or treatment to a cell, tissue, or organism, the product comprising a support material and a plurality of different nucleic acid molecules selected from cDNA molecules and single-stranded oligonucleotides, said nucleic acid molecules being attached to said support material, the nucleic acid molecules comprising [nucleic acid molecules containing] a sequence that is complementary to and specific for exon-exon or exon-intron junction regions of genes or RNAs that are spliced in a cell [treated by a reference toxic compound or treatment], said product comprising at least two nucleic acid molecules complementary to and specific for a distinct junction region of the same or a different gene or RNA, and said product allowing, when contacted with a sample containing nucleic acids under conditions allowing hybridisation to occur, the determination of the presence or absence of said junction regions in said sample.

74. (Previously Presented) The product of claim 72 or 73, wherein said plurality of different nucleic acid molecules is obtained by a method of identifying or cloning differentially spliced nucleic acids, said method comprising:

a) hybridizing a plurality of different RNAs derived from a first sample, wherein the composition or sequence of the RNAs is at least partially unknown, with a plurality of different cDNAs derived from a second sample, wherein the composition or sequence of the cDNAs is at least partially unknown; and

b) identifying or cloning, from the hybrids formed in a), a population of nucleic acids comprising an unpaired region, said cloned or identified nucleic acids comprising an unpaired region corresponding to portions of genes that are differentially spliced between said samples.

75. (Currently Amended) The product of claim 72, wherein said plurality of different nucleic acid molecules comprises single-stranded oligonucleotides comprising a sequence complementary to and specific for an exon or an intron retained or spliced in a cell [treated by a reference toxic compound or treatment], and wherein said oligonucleotides are obtained by a method comprising:

(a) identifying a splicing event characteristic of a cell [treated by a reference toxic compound or treatment] and determining the sequence of the spliced domain,

(b) synthesizing one or several single-stranded oligonucleotides complementary to and specific for said domain, and

(c) repeating steps (a) and (b) above with at least a second splicing event characteristic of a [said] toxic condition.

76. (Currently Amended) The product of claim 73, wherein said plurality of different nucleic acid molecules comprises single-stranded oligonucleotides comprising a sequence complementary to and specific for a junction region of a gene or RNA spliced in a cell [treated by a reference toxic compound or treatment], and wherein said oligonucleotides are obtained by a method comprising:

(a) identifying a splicing event characteristic of a cell [treated by a reference toxic compound or treatment] and determining the sequence of the spliced domain,

(b) synthesizing one or several single-stranded oligonucleotides complementary to and specific for a junction region formed by the splicing or absence of splicing of said domain and

(c) repeating steps (a) and (b) above with at least a second splicing event characteristic of a [said] toxic condition.

77. (Previously Presented) The product of claim 72 or 73, wherein the support material is selected from a filter, a membrane and a chip.

78. (Previously Presented) The product of claim 72 or 73, wherein the nucleic acid molecules comprise cDNA fragments.

79. (Previously Presented) The product of claim 72 or 73, wherein the nucleic acid molecules comprise single-stranded oligonucleotides.

80. (Currently Amended) A product for evaluating the therapeutic efficacy of a compound to a cell, tissue, or organism, the product comprising a support material and a plurality of different nucleic acid molecules selected from cDNA molecules and single-stranded oligonucleotides, said nucleic acid molecules being attached to said support material, the nucleic acid molecules comprising [nucleic acid molecules containing] a sequence that is complementary to and specific for introns or exons that are retained or spliced in a cell [treated by a reference therapeutic compound], said product comprising at least two nucleic acid molecules complementary to and specific for a distinct exon or intron of the same gene and said product allowing, when contacted with a sample containing nucleic acids under conditions allowing hybridisation to occur, the determination of the presence or absence of said exon or intron of said gene in said sample.

81. (Currently Amended) A product for evaluating the therapeutic efficacy of a compound to a cell, tissue, or organism, the product comprising a support material and a plurality of different nucleic acid molecules selected from cDNA molecules and single-stranded oligonucleotides, said nucleic acid molecules being attached to said support material, the nucleic acid molecules comprising [nucleic acid molecules containing] a sequence that is complementary to and specific for exon-exon or exon-intron junction regions of genes or RNAs that are spliced in a cell [treated by a reference therapeutic compound], said product comprising at least two nucleic acid molecules complementary to and specific for a distinct junction region of the same or a different gene or RNA, and said product allowing, when contacted with a sample containing nucleic acids under condition allowing hybridisation to occur, the determination of the presence or absence of said junction regions in said sample.

82. (Previously Presented) The product of claim 80 or 81, wherein said plurality of different nucleic acid molecules is obtained by a method of identifying or cloning differentially spliced nucleic acids, said method comprising:

a) hybridizing a plurality of different RNAs derived from a first sample, wherein the composition or sequence of the RNAs is at least partially unknown, with a plurality of different cDNAs derived from a second sample, wherein the composition or sequence of the cDNAs is at least partially unknown; and

b) identifying or cloning, from the hybrids formed in a), a population of nucleic acids comprising an unpaired region, said cloned or identified nucleic acids comprising an unpaired region corresponding to portions of genes that are differentially spliced between said samples.

83. (Currently Amended) The product of claim 80, wherein said plurality of different nucleic acid molecules comprises single-stranded oligonucleotides comprising a sequence complementary to and specific for an exon or an intron retained or spliced in a cell [treated by a reference therapeutic compound], and wherein said oligonucleotides are obtained by a method comprising:

(a) identifying a splicing event characteristic of a cell treated by a reference therapeutic

compound and determining the sequence of the spliced domain,

(b) synthesizing one or several single-stranded oligonucleotides complementary to and specific for said domain, and

(c) repeating steps (a) and (b) above with at least a second splicing event characteristic of said therapeutic condition.

84. (Currently Amended) The product of claim 81, wherein said plurality of different nucleic acid molecules comprises single-stranded oligonucleotides comprising a sequence complementary to and specific for a junction region of a gene or RNA spliced in a cell [treated by a reference therapeutic compound], and wherein said oligonucleotides are obtained by a method comprising:

(a) identifying a splicing event characteristic of a cell treated by a reference therapeutic compound and determining the sequence of the spliced domain,

(b) synthesizing one or several single-stranded oligonucleotides complementary to and specific for a junction region formed by the splicing or absence of splicing of said domain and

(c) repeating steps (a) and (b) above with at least a second splicing event characteristic of said therapeutic condition.

85. (Previously Presented) The product of claim 80 or 81, wherein the support material is selected from the group consisting of a filter, a membrane and a chip.

86. (Previously Presented) The product of claim 80 or 81, wherein the nucleic acid molecules comprise cDNA fragments.

87. (Previously Presented) The product of claim 80 or 81, wherein the nucleic acid molecules comprise single-stranded oligonucleotides.

88. (Previously Presented) A product for evaluating the responsiveness of a subject to a compound or treatment, the product comprising a support material and a plurality of different

nucleic acid molecules selected from cDNA molecules and single-stranded oligonucleotides, said nucleic acid molecules being attached to said support material, the nucleic acid molecules comprising nucleic acid molecules containing a sequence that is complementary to and specific for introns or exons that are retained or spliced in a cell from a responsive subject treated by a reference therapeutic compound or treatment, said product comprising at least two nucleic acid molecules complementary to and specific for a distinct exon or intron of the same gene and said product allowing, when contacted with a sample containing nucleic acids under condition allowing hybridisation to occur, the determination of the presence or absence of said exon or intron of said gene in said sample.

89. (Previously Presented) A product for evaluating the responsiveness of a subject to a compound or treatment, the product comprising a support material and a plurality of different nucleic acid molecules selected from cDNA molecules and single-stranded oligonucleotides, said nucleic acid molecules being attached to said support material, the nucleic acid molecules comprising nucleic acid molecules containing a sequence that is complementary to and specific for exon-exon or exon-intron junction regions of genes or RNAs that are spliced in a cell from a responsive subject treated by a reference therapeutic compound or treatment, said product comprising at least two nucleic acid molecules complementary to and specific for a distinct junction region of the same or a different gene or RNA, and said product allowing, when contacted with a sample containing nucleic acids under conditions allowing hybridisation to occur, the determination of the presence or absence of said junction regions in said sample.

90. (Previously Presented) A product comprising a support material and a plurality of different oligonucleotides specific for alternative exons or introns of a gene, wherein the oligonucleotides are attached to the support material, and wherein the oligonucleotides are prepared by:

(a) identifying a splicing event characteristic of a physiopathological condition and determining the sequence of the spliced domain,

(b) synthesizing one or several oligonucleotides complementary to and specific for said

domain, and

(c) repeating steps (a) and (b) above with at least a second splicing event characteristic of said physiopathological condition.

91. (Previously Presented) A product comprising, immobilized on a support material, a nucleic acid library comprising a plurality of nucleic acid molecules, wherein each of said nucleic acid molecules comprises a sequence corresponding to a portion of a gene which is differentially spliced between two physiological conditions of a cell or tissue, said library being enriched for said nucleic acid molecules.

92. (Previously Presented) A product comprising, immobilized on a support material, a nucleic acid library comprising a plurality of oligonucleotide pairs, each pair of oligonucleotides comprising a first and a second oligonucleotide, wherein said first and second oligonucleotides of each of said pairs comprise sequences corresponding to differentially spliced forms of a gene, said library being enriched for said pairs.

93. (Previously Presented) A product comprising, immobilized on a support material, a microorganism library comprising microorganisms transformed by a nucleic library of claim 91.

94. (New) A method of producing a product comprising a support material and a plurality of different nucleic acid molecules, wherein said method comprises:

(a) providing a plurality of at least two cDNA molecules or single-stranded oligonucleotides comprising a sequence which is complementary to and specific for distinct exons or introns of a gene or RNA and which correspond to a region of variability due to differential splicing of said gene or RNA, and

(b) immobilizing said plurality of cDNA molecules or single-stranded oligonucleotides to a support material,

said product allowing, when contacted with a sample containing nucleic acids under conditions allowing hybridisation to occur, the determination of the presence or absence of said exon or

intron of said gene or RNA in said sample.

95. (New) The method of claim 94, comprising providing a plurality of at least two single-stranded oligonucleotides of between 5 and 100 bases in length comprising a sequence that is complementary to and specific for a distinct exon-exon or exon-intron junction region of a same or different gene or RNA.

96. (New) The method of claim 95, wherein the single-stranded oligonucleotides are less than 50 bases in length.

97. (New) The method of claim 94, wherein providing said plurality of different nucleic acid molecules comprising cDNA molecules comprises:

(a) hybridizing a plurality of different RNAs derived from a first sample, wherein the composition or sequence of the RNAs is at least partially unknown, with a plurality of different cDNAs derived from a second sample, wherein the composition or sequence of the cDNAs is at least partially unknown, and

(b) identifying or cloning, from the hybrids formed in (a), a population of nucleic acid molecules comprising an unpaired region, said cloned or identified nucleic acid molecules comprising an unpaired region corresponding to portions of genes that are differentially spliced between said samples.

98. (New) The method of claim 94, wherein providing said plurality of different nucleic acid molecules comprising single-stranded oligonucleotides comprises:

(a) identifying a splicing event characteristic of a physiopathological condition and determining the sequence of the spliced domain,

(b) synthesizing one or several single-stranded oligonucleotides complementary to and specific for said domain, and

(c) repeating steps (a) and (b) above with at least a second splicing event characteristic of said physiopathological condition.

99. (New) The method of claim 95, wherein providing said plurality of different nucleic acid molecules comprising single-stranded oligonucleotides comprises:

(a) identifying a splicing event characteristic of a physiopathological condition and determining the sequence of the spliced domain,

(b) synthesizing one or several single-stranded oligonucleotides complementary to and specific for a junction region formed by the splicing or absence of splicing of said domain and

(c) repeating steps (a) and (b) above with at least a second splicing event characteristic of said physiopathological condition.

100. (New) The method of claim 94, wherein the support material is selected from a filter, a membrane, and a chip.

101. (New) The method of claim 94, wherein the cDNA molecules or oligonucleotides are specific of alternative splicings representative of a cell or tissue in a given pathological condition.

102. (New) The method of claim 101, wherein the cDNA molecules or oligonucleotides are specific of alternative splicings representative of a tumor cell or tissue.

103. (New) The method of claim 101, wherein the cDNA molecules or oligonucleotides are specific of alternative splicings representative of a cell or tissue undergoing apoptosis.